DETAILED ACTION

Applicant's response of January 29, 2008, to the Restriction Requirement dated November 29, 2007 has been entered. No claims were amended, cancelled or newly added. Claims 1-33 are pending in the Application.

Response to Election/Restrictions

Applicants' election of Group I (claims 1-8), drawn to an immature immunodeficient non-human mammal into which human-derived hematopoietic cells have been transplanted, is acknowledged. Applicants' species election of mouse as the non-human mammal, cord blood as the source of hematopoietic cells, T cells as immunocompetent cells and IgG as the immunoglobulin, is further acknowledged. Applicants should note that in view of the teachings of the prior art of record, the restriction between the species of T cells and B cells, and between the species of cord blood and peripheral blood is hereby withdrawn. The election was made with traverse.

The traversal is on the grounds that the Examiner has already made a conclusion of unpatentability by citing the reference by Ishikawa et al. and determining that the claims do not contribute a special technical feature over this reference and thus dividing the claims into 8 different groups; concluding that the restriction requirement is improper. Applicants' arguments have been fully considered, but are not found to be persuasive.

The instant Application is a 371 national stage entry of PCT/JP04/08784. As such, the claims therein have been properly restricted under the rules of Unity of Invention, and not solely based on U.S. restriction practice. PCT Rule 13.2, as it was modified effective July 1, 1992, no longer specifies the combinations of categories of invention which are considered to have unity of invention. The categories of invention in former PCT Rule 13.2 have been replaced with a statement describing the method for determining whether the requirement of unity of invention is satisfied. Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. In the instant case, the inventions of Groups I-VII (not 8) are distinct, each from the other, and as indicated in the restriction requirement, the Groups are linked by the special technical feature that is an immature

immunodeficient non-human mammal into which human-derived hematopoietic cells have been transplanted. The claims fail to provide a contribution over the prior art, because Ishikawa et al. teach the long-term engrafting of human hematopoietic cells into newborn NOD/SCID/β2-microglobulin deficient mice. As stated in MPEP 1850, under Unity of Invention, PCT Rule 13.2, "Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features".

The restriction under PCT rules13.1 and 13.2 is proper, and Applicants have not provided any evidence or arguments that Ishikawa et al. has been improperly applied. Furthermore, according to MPEP 1893.03(d), any nonelected processes of making and/or using an allowable product will be considered for rejoinder following the practice set forth in MPEP § 821.04(b).

The requirement for restriction is deemed proper, maintained and hereby made FINAL. Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

The instant claims have been examined commensurate with the scope of the elected invention and the species of the elected invention. Applicant timely responded to the restriction (election) requirement in the reply filed January 29, 2008.

Claims 1-8 are under current examination.

Information Disclosure Statement

The information disclosure statement filed 12/15/2005 fails to comply with 37 CFR 1.98(a)(3)(ii), which requires a copy of the translation if a written English-language translation of a non-English-language document, or portion thereof, is within the possession, custody, or control of, or is readily available to any individual designated in § 1.56(c). It has been placed in

the application file, but the information referred to therein has not been fully considered, since JP 6-500233 is in the Japanese language.

Objection to Specification

The brief description of the drawings corresponding to Figures 1-12 are objected to, because each of the Figures contain multiple alphabetically labeled panels, each containing separate data, that are not described in the corresponding brief description. For example, Figure 1A contains panels a-d, not identified in the brief description; Figure 3 contains panels a-e, also not described; etc. Appropriate correction is required in the brief description for each of Figures 1-12.

Claim Objection

Claim 1 is objected to for employing incomplete sentence structure.

Claim 1 recites the limitation "to generate immunocompetent cells derived from said human", in the third line. Amending the claim to recite "to generate immunocompetent cells derived from said human-derived hematopoietic cells" would be considered remedial.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002; of record).

The claims embrace an immature immunodeficient mouse into which human cord blood hematopoietic cells have been transplanted, and which is able to generate T cells from said human cells.

Ishikawa et al. teach long-term xenogeneic engrafting of cord blood human hematopoietic cells into newborn NOD/SCID/β2-microglobulin deficient mice (Title and Abstract; limitation of claims 1, 3, 4 and 8). Further teaching multilineage engraftment, and that high levels of engraftment were primarily by T cells (first column, p. 490 and Figure 1; limitation of claim 5). With reference to previously published results by Kollet et al., the authors additionally teach that because the duration of engraftment was relatively short, backcrossing onto other strains of mice may be needed for longevity, constituting breeding of the immature immunodeficient mouse (limitation of claim 2).

Therefore by teaching all the limitations of claims 1-5 and 8, Ishikawa et al. anticipate the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6 and 7 are rejected under 35 U.S.C. §103(a) as being unpatentable over Ishikawa et al. (Am. J. Transpl. 2:520-525, 2002; of record), in view of Olive et al. (Immunol. Cell Biol. 76:520-525, 1998).

The claims embrace an immature immunodeficient mouse into which mature human hematopoietic cells have been transplanted, and which is able to generate IgG immunoglobulin from said human cells.

Ishikawa et al. teach long-term xenogeneic engrafting of cord blood human hematopoietic cells into newborn NOD/SCID/β2-microglobulin deficient mice (Title and Abstract; limitation of claims 1, 3, 4 and 8). Further teaching multilineage engraftment, that included cells bearing the CD19 pan-specific B cell marker (Table 1, p. 492; limitation of claim 1).

While Ishikawa et al. do not describe detecting IgG in the recipient newborn mice, the production of human IgG in xenografted immunodeficient mice was well known in the prior art. Olive et al. describe the successful engraftment of human peripheral blood lymphocytes in SCID mice, determined by measurement of human IgG in mouse sera, that continued to increase for 8 weeks, in addition to T cell engraftment in lymphoid tissues (Title and Abstract; limitation of claims 6 and 7); thus curing the deficiency of IgG in Ishikawa et al.

Ishikawa et al. state that the number of cells that were planted per newborn mouse is less than the larger graft size previously reported in earlier studies (second column, p. 493), thus providing the motivation to use immature mice instead of the 8 week old mice utilized by Olive et al.

The teachings of Ishikawa et al. and Olive et al. are both directed to engraftment of human hematopoietic cells in immunodeficient mice. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings and to introduce human hematopoietic cells into immature immunodeficient mice to produce human B cells and IgG, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to use the immature immunodeficient mouse of Ishikawa et al. for human hematopoietic cell engraftment, because such would require a smaller graft size.

Conclusion

Claims 1-8 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633